STRATEGIC OBJECTIVE 4

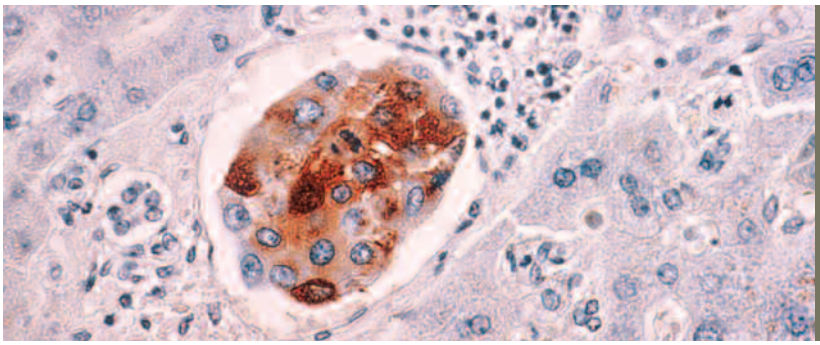
Develop Effective and Efficient Treatments

We will support the development and dissemination of interventions to treat malignancy by either destroying all cancer cells or modulating and controlling metastasis, both with minimal harm to healthy tissue.

Developing more efficient and effective cancer treatments that leave surrounding healthy tissue unharmed is at the heart of NCI's research agenda. These efforts build on our accelerated progress in preventing cancer and complement our increasing ability to thwart the progression of cancer to a metastatic state. Individualized therapies tailored to the specific characteristics of a patient's cancer provide hope that some cancers can be cured and many others managed as chronic diseases with little or no adverse effect on the daily lives or life expectancy of patients.

A strong understanding of the fundamental mechanisms leading to cancer progression and metastasis will dramatically improve our ability to identify key biochemical events in the disease process as targets for treatment. Accelerating target validation and the development of new treatment modalities will be possible through recent advances in biomedical technologies such as genomics, proteomics, metabolomics, nanotechnology, and imaging. Rapid translation from development to delivery will ensure that promising therapeutics move safely and efficiently from preclinical development through late-stage clinical trials and into clinical practice.

As with prevention and early detection research, we must anticipate scientific and technological advancements and enhance clinical research with interdisciplinary collaborations and a focus on translation into clinical practice. We must promote new and ongoing communication networks among researchers, oncologists, industry, and patient advocates and provide clinical trial investigators with a common clinical trials informatics platform. A highly interactive and optimally coordinated cancer clinical trials system will facilitate the effective conduct of small Phase I clinical trials for safety and efficacy, improve prioritization and coordination of large Phase II and III trials that test the efficacy of treatment for specific types of cancer, and remove barriers to the testing and use of combinations of treatment modalities.



STRATEGY 4.1 — Identify the molecular and cellular determinants of metastatic behavior.

Despite improved outcomes for many cancer types, patients with disseminated or metastatic cancer continue to have the poorest survival rates for all cancers. To change this reality, cancer researchers must gain new insights into the fundamental differences between metastatic and non-metastatic cancer. Recent advances in genetic profiling of tumors has led to the identification of several "metastatic expression profiles" present in the primary tumor, suggesting the existence of inherent genetic distinctions that can be used to identify tumors capable of metastatic behavior. Better animal models for studying metastatic behavior have also been developed. NCI will:

- Build on these advances by developing animal models for identifying relevant targets for treating metastatic cancers.
- Develop an easily accessible database of genes and signaling pathways that have been identified in multiple cancer models and species and validated as participants in the metastatic process.
- Support research to gain a better understanding of tumor stem cells and their role in human cancer at the molecular and functional level.

This coordinated investment will help expedite new insights into fundamental processes driving metastasis and enable identification of novel therapeutic targets and agents to preempt or control metastatic tumors.

STRATEGY 4.2—Validate cancer biomarkers for cancer prognosis, metastasis, treatment response, and cancer progression.

For most cancers, successful prevention depends on accurate risk assessment and successful treatment depends on early detection. Pioneering proteomic and biomarker advances and the promise of nanotechnology give us new hope for improved monitoring of cancer progression, metastasis, and treatment response. Improved biomarkers are crucial in ensuring that patients receive the treatments most likely to be successful in providing the best possible opportunity for survival. NCI will:

- Identify the proteins associated with cancers and employ recent advances in molecularly targeted imaging to locate very small tumors and interrogate their molecular features to assess prognosis.
- Refine and utilize high-throughput validation techniques to identify biomarkers for cancer prognosis, progression, metastasis, and treatment response.
- Create a library of validated biomarkers and make it available to the cancer research community.

STRATEGY 4.3—Accelerate identification, development, and validation of potential targets and strategies for cancer treatment by integrating preclinical and clinical research.

NCI will provide the leadership to turn molecular biology discoveries into valid, credentialed targets and to move the most promising preclinical leads to clinical testing. We will invest in effective infrastructures to promote a high degree of integration, coordination, and

communication along the discovery-development-delivery research continuum. Participants in all phases of research will need access to state-of-the-art enabling technologies. NCI will:

- Strengthen regional infrastructure to integrate preclinical science and early clinical testing. For example, NCI will facilitate the collaboration of clinical scientists, cancer modelers, and imaging researchers to develop novel imaging techniques for the preclinical assessment of specific targeted treatment agents that will enter clinical trials.

- Support cancer modeling and translational research to devise new preclinical tactics to identify biomarkers for assessing the efficacy, mechanism of action, and toxicity of promising treatment agents.
- Support preclinical researchers in the development of new imaging agents and approaches to overcoming important challenges to clinical research.
- Leverage NCI resources to establish public-private partnerships to expedite the selection of agents for movement into clinical testing.
- Augment the existing clinical trials bioinformatics infrastructure to give preclinical and clinical researchers easy access to the basic science knowledge they need for their studies.
- Link preclinical research data with a comprehensive database of clinical trial results to coordinate and optimize information and data sharing.

This integration and support for the preclinical and clinical testing of cancer interventions will accelerate selection and development of candidate treatment agents that are highly effective, less costly, and most likely to benefit patients.

New Nanotechnology Characterization Laboratory Supports Cancer Research and Development

NCI is engaged in an unprecedented effort to leverage the resources of government, industry, and academia in harnessing the power of nanotechnology to radically change the way we diagnose, treat, and prevent cancer. One initiative involves working in concert with the National Institute of Standards and Technology and the U. S. Food and Drug Administration to establish the Nanotechnology Characterization Laboratory (NCL). Scientists at the NCL perform preclinical efficacy and toxicity testing of nanoparticles and serve as a national resource and knowledge base to facilitate the regulatory review of nanotechnologies intended for cancer therapies and diagnostics. By providing the critical infrastructure and characterization services to nanomaterial providers, the NCL will accelerate the transition of basic nanoscale particles and devices for the development of new diagnostics, therapeutics, and preventives.

STRATEGY 4.4 — Develop a balanced approach for managing the toxicities of cancer therapy.

Minimizing the toxic effects of cancer treatment is critical to reducing morbidity and mortality. NCI will focus on developing molecularly targeted drugs that have fewer of the nonspecific, cytotoxic side effects that are commonly associated with traditional chemotherapeutic agents. We will:

- Support the concurrent development of tumor profiling devices such as gene or protein microchip arrays to inform the patient-specific selection of targeted therapies that will maximize patient response and minimize unwanted side effects.
- Foster the development of mechanisms for low-dose, site-specific drug delivery, such as aerosols that deliver agents to the lung and antibodies that selectively target drugs to cancer cells.
- Support the development of systems cell biology and computational modeling approaches to identify multiple cellular pathways that contribute to carcinogenesis and metastasis and that can be treated with low-dose, well-tolerated targeted drug combinations that uniquely affect cancer cells and spare normal cells.
- Invest in research to address the unwanted side effects caused by many useful, single-agent targeted therapies.
- Work with other NIH Institutes and Centers to better understand normal tissue toxicity and to identify and address gaps in research relevant to cancer treatment toxicity.
- Leverage initiatives under development at other Federal agencies that focus on toxicity assessments using nanotechnology, proteomics, genomics, metabolomics, and other advanced technologies.
- Support the application of these toxicology prediction techniques to minimize chemotherapy-induced collateral toxicity to organs not affected with cancer.

Minimizing toxicities will make it possible for more patients to complete therapeutic regimens and maximize the benefits of treatment.

STRATEGY 4.5—Integrate clinical trial structures to ensure expedited identification of the most promising treatment opportunities, rapid execution of the necessary clinical trials, and effective utilization of information and resources by clinicians.

Researchers have made substantial progress in developing new, more effective cancer therapeutics over the past thirty years. The timely development of even more sophisticated treatment approaches based on the molecular characteristics of a patient's tumor will require a restructured clinical trial enterprise. NCI will:

- Build new partnerships and multidisciplinary collaborations to ensure the unprecedented level of integration required to realize the tremendous potential for improved cancer treatments arising from current scientific advances.
- Coordinate and optimize patient-information and other data sharing by creating a comprehensive database of clinical trials and results.
- Create an integrated infrastructure to accelerate high-priority clinical trials implementation and eliminate redundancy.
- Develop patient recruitment strategies to ensure sufficient levels of participation from targeted populations.
- Collaborate with industry and healthcare providers to ensure that cancer patients have access to the best treatment available.
- Build on advanced technologies to assess the effects of drugs on molecular targets and pathways. Incorporate relevant biology studies into clinical trials to maximize our understanding of drug mechanisms and target effects in the context of human treatment.
- Create new partnerships and collaborations to accelerate the creation, development, validation, and utilization of these critical assays and tools.
- Rapidly deploy these resources in clinical trials of new agents and apply the knowledge gained to develop subsequent agents.

Greater integration of clinical trial components will accelerate the movement of effective interventions through clinical testing and set the stage for moving these interventions into public health and clinical practice.